UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO

SANTA BARBARA • SANTA CRUZ

15
3.15.05 MB

RITA F. REDBERG, M.D., M.Sc., F.A.C.C.
Professor of Medicine
Director, Women's Cardiovascular Services
UCSF National Center of Excellence in Women's Health
505 Parnassus Ave., Suite M-1180
School of Medicine, Division of Cardiology
San Francisco, California 94143-0124

PHONE: 415-476-6874
FAX: 415-502-8627
E-MAIL: redberg@medicine.ucsf.edu

March 1, 2005

Stephen Galson, MD
Acting Director of the Center for Drug Evaluation and Research
US Food and Drug Administration
5600 Fishers Lane
Mail Stop HFD-110
Rockville MD 20857-0001

RE: Citizens Petition concerning glycoprotein IIb/IIIa inhibitors – tirofiban, lamifiban, eptifibatide, and abciximab for acute coronary syndromes in women

Dear Dr. Galson:

We are writing to request that the FDA revise the labeling on glycoprotein IIb/IIIa inhibitors – tirofiban, lamifiban, eptifibatide, and abciximab - to reflect the adverse event risk (death and myocardial infarction) in women when these agents are used for acute coronary syndrome in women not routinely scheduled to undergo early coronary revascularization and to request that the FDA hold an advisory committee meeting on this subject. The grounds for this request is adverse safety data concerning the use of glycoprotein IIb/IIIa inhibitors for acute coronary syndromes (ACS) in women. A meta-analysis of six large clinical trials of the clinical efficacy and safety of glycoprotein IIb/IIa inhibitor use in 31,402 patients (35% women) showed that while there was a mortality benefit in men for use of these agents, there was a 15% increase in death and myocardial infarction (MI) with use of these drugs in women. [1] This 15% increase was statistically significant and is of clinical concern. The sex difference in treatment effect remained ($p<0.0001$) after adjustment of baseline differences. A post hoc analysis of these data, limited to the sub-group of women with increased troponin levels (n=1,506) suggests a non-significant trend towards benefit with an odds ratio of 0.93 (95% CI .68 – 1.28). Attached to this letter is a copy of the review article from Lancet summarizing this data regarding the use of glycoprotein IIb/IIIa inhibitors in women with ACS. There was a pooled analysis of data on abciximab used in the setting of percutaneous coronary intervention in 1,771 women (6,595 total patients) that did not find a gender difference in the one year combined endpoint of death, myocardial infarction and urgent revascularization. [2] This study used a different clinical setting and different clinical endpoint than the larger Boersma study. To the best of our knowledge, this petition includes all information relevant to the use of glycoprotein IIb/IIIa inhibitors in acute coronary syndromes.

2005P-0107

CP 1

I am concerned that current usage of glycoprotein IIb/IIIa inhibitors for women with acute coronary syndromes is leading to avoidable death and myocardial infarction, and this risk should be reflected in the labeling. I met with Dr. Stockbridge and staff from the Office of Women's Health at the FDA last year concerning cardiovascular drugs in women and this topic was discussed as part of that meeting.

As a practicing cardiologist and Director of Women's Cardiovascular Services at the University of California, San Francisco Medical Center, as well as Director of a Continuing Medical Education Course on Heart Disease in Women for the American College of Cardiology, Science Advisor for the American Heart Association's Choose to Move Program for Women and member of the WomenHeart Scientific Adviosry Board, I have followed the area of cardiovascular drugs in women for over a decade. These agents were approved for the indication of treatment of patients with acute coronary syndrome, including patients who are to be managed medically as well as those undergoing percutaneous coronary intervention. It is clear that there are gender differences in heart disease and it is crucial that our pharmacologic management reflect our best knowledge of these differences.

I suggest that FDA convene an advisory committee meeting on the topic of cardiovascular drugs in women. I would be happy to present information at this meeting and to be a resource for identifying other scientists and clinicians who could contribute to the discussion. This advisory committee meeting could review existing data with the intent to formulate recommendations to guide care of women. I am aware that the Office of Women's Health was directed in FY05 to focus on women and cardiovascular disease. Thus, this seems to be an ideal time to follow up on these issues of cardiovascular drug use in women that we discussed at my meetings at FDA last year and to ensure we are offering optimal cardiovascular care to all patients. In this regard, an advisory committee meeting on the subject would be most helpful. I would be happy to discuss this further with your agency.

Sincerely,

Rita F. Redberg

Rita F. Redberg, MD, M.Sc., FACC
Professor of Medicine
Director, Women's Cardiovascular Services
UCSF National Center of Excellence in Women's Health
WomenHeart Scientific Advisory Board Member

cc:
Susan Wood, PhD, FDA, Director of the Office of Women's Health
Norman Stockbridge, MD, FDA Acting Division Director, Division of Cardio-Renal Drug Products
Paul J. Seligman, MD, MPH, FDA, Acting Director, Office of Drug Safety

Supported by:

Susan Bennett, MD, FACC
Clinical Director
Women's Heart Program, George Washington Univ. Hospital
WomenHeart Scientific Advisory Board Member

Sharonne Hayes, MD, FACC
Director, Women's Heart Clinic
Mayo Clinic
WomenHeart Scientific Advisory Board Chairperson

Kathy Berra, RN
Clinic Coordinator
Stanford University
WomenHeart Scientific Advisory Board Member

Pam Marcovitz, MD, FACC
Director, Clinical Cardiology Fellowship Program
Director, Ministrelli Women's Heart Center
William Beaumont Hospital
WomenHeart Scientific Advisory Board Member

REFERENCES

1. Boersma E, Harrington RA, Moliterno DJ, White H, Theroux P, Van de Werf F, de Torbal A, Armstrong PW, Wallentin LC, Wilcox RG, Simes J, Califf RM, Topol EJ, Simoons ML. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. *Lancet.* 2002;359:189-98.
2. Cho L, Topol EJ, Balog C, Foody JM, Booth JE, Cabot C, Kleiman NS, Tcheng JE, Califf R, Lincoff AM. Clinical benefit of glycoprotein IIb/IIIa blockade with Abciximab is independent of gender: pooled analysis from EPIC, EPILOG and EPISTENT trials. Evaluation of 7E3 for the Prevention of Ischemic Complications. Evaluation in Percutaneous Transluminal Coronary Angioplasty to Improve Long-Term Outcome with Abciximab GP IIb/IIIa blockade. Evaluation of Platelet IIb/IIIa Inhibitor for Stent. *J Am Coll Cardiol.* 2000;36:381-6.

TO: Lyle Jaffe
US Food and Drug Administration
5600 Fishers Lane
Rockville MD 20857-0001
FAX 301 827 6870

3133 5 [illegible]

FROM: Rita F. Redberg, MD, Msc.

RE: Addendum to Citizen's Petition Concerning labeling of labeling on glycoprotein IIb/IIIa inhibitors – tirofiban, lamifiban, eptifibatide, and abciximab

Certification: To the best of my knowledge, this petition includes all information relevant to the petition, favorable or not.

Environmental impact – In accordance with categorical exclusions, per CFR 25.30 an environmental impact statement is not needed with this petition.

Thank you